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Iqbal Grewal

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EXAMINER

GAMBEL, PHILLIP

ART UNIT

PAPER NUMBER

1644

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DELIVERY MODE

11/29/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/099,818

Applicant(s)

GREWAL, IQBAL

Examiner

Phillip Gambel

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 12 September 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-11, 13-30 and 32-49 is/are pending in the application.
- 4a) Of the above claim(s) 19 and 40-45 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11, 13-18, 32-39, 46-49 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- ☐ Notice of Informal Patent Application
- ☐ Other: \_\_\_\_\_

### DETAILED ACTION

1. Applicant's amendment, filed 09/12/2007, has been entered.

Claims 1, 14-15, 17-19 and 32-33 have been amended.

Claims 35-49 have been added.

Claims 12 and 20-31 have been canceled.

Claims 1-11, 13-30 and 32-49 are pending.

Newly submitted claims 40-45 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Newly submitted claims 40-45 are drawn to methods of further administering a cytotoxic or chemotherapeutic agent, including cytotoxic conjugates of CD40-specific / CD20-specific antibodies previously not claimed.

The newly submitted claims encompass the administration of cytotoxic or chemotherapeutic agents that differ in structure and function from the combination of anti-CD40 antibodies / anti-CD20 antibodies previously elected in the claimed methods of treating a neoplastic disease or disorder.

Further, the cytotoxic conjugates of CD40-specific / CD20-specific antibodies would differ from the previously elected CD40-specific / CD20-specific antibodies, including CD40-specific antibodies that stimulate CD40;

given that the modes of action of cytotoxic antibody conjugates would be expected to kill CD40-expressing neoplastic cells, rather than treating neoplastic diseases or disorders via the stimulation of CD40, as currently recited in the amended claims.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Given these differences between the newly submitted cytotoxic and chemotherapeutic agents, including cytotoxic antibody conjugates and the previous prosecution on methods employing CD40-specific antibodies and CD20-specific antibodies in the absence of cytotoxic and chemotherapeutic agents or cytotoxic antibody conjugates and the non-coextensive searches based upon such differences, newly submitted claims 40-45 have been withdrawn from consideration as being drawn to the non-elected species based upon original presentation.

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Further, it is noted that applicant has submitted these claims after a first Office Action after filing a RCE as well.

Applicant had the opportunity to submit these newly added limitations at the time the request for continued examination was filed.

Therefore, given the above, including issues under the various patent statutes and how they would apply to methods versus product claims; one or more of the following reasons apply, as indicated in the previous Office Action:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph

The newly submitted claims would be subject to election of species.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits.

Accordingly, claims 19 and 40-45 are withdrawn from consideration as being directed to a non-elected invention or species. See 37 C.F.R. 1.142(b) and M.P.E.P. 821.03.

As pointed out previously, applicant's election of Group I and the species of a CD40-specific antibody and a CD20-specific antibody as well as multiple myeloma in the reply filed on 11/14/2005 has been acknowledged.

Also, consistent with the previous indication, claims 1-11, 13-18, 32-39 and 46-49 are under consideration in this application as they read on CD40-specific antibodies and CD20-specific antibodies as the specific agents as well as the various neoplastic diseases claimed in the interest of compact prosecution.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Action will be in response to applicant's amendment, filed 09/12/2007.

The rejections of record can be found in the previous Office Action, mailed 03/12/2007.

3. Given applicant's newly added claims drawn to the SGN-14 anti-CD40 antibody and rituximab, the following of record is noted herein.

Also, see applicant's amendment, filed 10/05/2006 with respect to the S2C6 antibody described in WO/0075348 (e.g., see page 19, paragraph 2 and page 20, paragraph 1 of the instant specification) and to rituximab described in U.S. Patent No. 5,736,137 (E.g., see page 21, paragraph 1 of the instant specification).

It is noted that the anti-CD40 antibody S2C6 is also referred to as SGN-14 and described in WO/007538 (e.g., see Example I on pages 44-46 of the instant specification).

Also, see U.S. Patent No. 5,736,137 (Anderson et al., anti-CD20 antibody) and U.S. Patent No. 6,843,989 (Siegall et al., anti-CD40 antibody) for satisfying the requirements for the deposit of biological materials under 35 U.S.C. § 112, first paragraph.

5. Objections to the Claims: Proper Designations.

(A) Claims 37-38 are objected to because the ATCC Accession No. 69119 refers to the S2C6 antibody and not to the SGN-114, as currently recited.

See page 5 paragraph 3 of Siegall et al., WO/0075348.

(B) Claim 39 is objected to because the "rutuximab" should be "rituximab".

(C) Claims 47 and 49 are objected to because "F(ab')<sub>2</sub>" should be "F(ab')<sub>2</sub>".

6. Given applicant's amended claims, the previous rejections under 35 U.S.C. § 112, second paragraph and 35 U.S.C. § 112, first paragraph, written description / new matter with respect to the recitation of "an effective amount of a combination of a CD40 specific binding agent and a CD20 specific binding agent, ..." have been withdrawn.

7. Claims 1-11, 13-18, 32-33 and newly submitted claims 34-35 and 46-49 are rejected under 35 U.S.C. § 102(e) as anticipated by Hanna et al. (US 2001/0018041 A1) (see entire document) and

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in further evidence of Armitage et al. (U.S. Patent No. 5,674,492 cited in paragraphs [0013] and [0104] of Hanna et al.), wherein said teachings of agonistic anti-CD40 are acknowledged by page 2, paragraph 1 of the instant specification and paragraphs [0005] and [0036] of Fanslow et al., US 2005/0129689 A1) essentially for the reasons of record.

Applicant's arguments, filed 09/12/2007, in conjunction with certain legal citations, have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant argues that Hanna et al. requires the use of an anti-CD40L antibody antagonists, wherein applicant's claims as amended do not require a CD40L antagonist as defined by the prior art.

However, as pointed out previously, Hanna is not limited to the use of anti-CD40L antibody antagonists (as apparently defined and asserted by applicant) to treat malignancies.

Again, applicant is reminded that Hanna also contemplates the particular combination of anti-CD20 antibodies and anti-CD40 antibodies. See paragraph [0104] on page 10 of Hanna.

Paragraphs [0013] and [0104] of Hanna et al. contemplates the anti-CD40 antibodies taught by Armitage et al. (U.S. Patent No. 5,674,492).

Armitage et al. teach anti-CD40 antibodies, including the M2 and M3 antibodies (See entire document).

For example, page 2, paragraph 1 of the instant specification discloses that:

"CD40 stimulation by mAb M2 and M3 inhibits growth of several B-cell lymphomas and induces regression of several B-cell lymphomas and induces regression of established tumors in vivo (Funakoshi et al., (1994) Blood 83: 2787-2794; Funakoshi et al. J. Immunol., (1996) 19: 93-101).

Fanslow et al. US 2005/0129689 A1) describes the antibodies referenced in U.S. Patent No. 5,674,492, namely the M2 and M3 antibodies as agonistic anti-CD40 antibodies as those antibodies that mimic the biological effects of CD40L are useful in the treatment of disease characterized by neoplastic cells that express CD40 such as B lymphomas, melanomas and carcinomas,

Again, certain anti-CD40 antibodies referenced by Hanna et al. are the same anti-CD40 antibodies taught by U.S. Patent No. 5,674,492, which is referenced in paragraphs [0013] and [0104] of Hanna et al.

Therefore, in contrast to applicant's assertions that Hanna et al. does not teach anti-CD40 antibodies that stimulate CD40, as currently recited in the instant claims,

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Hanna et al. does teach the use of agonistic anti-CD40 antibodies that can stimulate CD40, as currently recited in the instant claims, including its combination with anti-CD20 antibodies, in the treatment of B cell lymphomas and leukemias.

Applicant does not appear to address or distinguish the teachings of Hanna's teaching of agonistic anti-CD40 antibodies M2 and M3 from the description of the instant specification of the same M2 and M3 antibodies that can inhibit the growth of several B-cell lymphomas and induces regression of several B-cell lymphomas and induces regression of established tumors in vivo application.

Products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Therefore, Hanna et al. does teach the use of anti-CD40 antibodies, including its combination with anti-CD20 antibodies, in the treatment of B cell lymphomas and leukemias.

For the purposes of searching for and applying prior art under **35 U.S.C. 102 and 103**, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG Industries v. Guardian Industries, 48 USPQ2d 1351, 1355 (Fed. Cir. 1998).

It is noted that the claimed methods recite "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts.

See MPEP 2111.03.

Further, it is noted the current claims recited further comprising cytotoxic and chemotherapeutic agents as well as cytotoxic antibody conjugates that differ in structure and modes of action from antibodies that stimulate CD40 in the claimed methods of treating neoplastic diseases and disorders.

Therefore, the instant claims are met by any prior teaching of combining anti-CD40L antibodies with anti-CD20 and anti-CD40 antibodies, as broadly encompassed by the claimed methods.

Applicant's arguments have not been found persuasive

The following of record is reiterated for applicant's convenience.

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Hanna et al. teach methods of treating B cell lymphomas and leukemias, including non-Hodgkin's lymphoma (NHL) (e.g. see paragraphs [0090] – [0101]) with the combination of CD40-specific antibodies (e.g. see CD40L Antagonists in paragraphs [0036] – [0078], and CD20-specific antibodies, including the C2B8 antibody / Rituxan (e.g. see paragraph [0104]) (e.g. see paragraphs Summary of the Invention, including paragraph [0018]; Detailed Description of the invention, including paragraphs [0088], [0092], [0104] and [0113]; Claims). Although the prior art does not teach the CD40-specific S2C6 antibody per se, the inhibitory CD40-specific antibodies taught by the prior art would have the same CD40 binding characteristics under the broadest reasonable interpretation of CD40-binding antibodies in the absence of limitations to the contrary.

Hanna et al. teach recombinant antibodies and antibody fragments consistent with the newly submitted claims (e.g., see paragraphs [0025] – [0032] and [0037] – [0078], Hanna et al. teach such antibodies.

With respect to dosing regimens, Hanna et al. teach dosing regimens that were consistent and immediately envisaged as reading on the newly submitted limitation of sequentially (e.g., see paragraphs [0071] – [0076] and [0081] – [0088] ).

Paragraphs [0013] and [0104] of Hanna et al. contemplates the anti-CD40 antibodies taught by Armitage et al. (U.S. Patent No. 5,674,492).

Armitage et al. teach anti-CD40 antibodies, including the M2 and M3 antibodies (See entire document).

For example, page 2, paragraph 1 of the instant specification discloses that: "CD40 stimulation by mAb M2 and M3 inhibits growth of several B-cell lymphomas and induces regression of several B-cell lymphomas and induces regression of established tumors in vivo (Funakoshi et al., (1994) Blood 83: 2787-2794; Funakoshi et al. J. Immunol., (1996) 19: 93-101).

Fanslow et al. US 2005/0129689 A1) describes the antibodies referenced in U.S. Patent No. 5,674,492, namely the M2 and M3 antibodies as agonistic anti-CD40 antibodies as those antibodies that mimic the biological effects of CD40L are useful in the treatment of disease characterized by neoplastic cells that express CD40 such as B lymphomas, melanomas and carcinomas,

Again, certain anti-CD40 antibodies referenced by Hanna et al. are the same anti-CD40 antibodies taught by U.S. Patent No. 5,674,492, which is referenced in paragraphs [0013] and [0104] of Hanna et al.

Therefore, Hanna et al. does teach the use of anti-CD40 antibodies, including its combination with anti-CD20 antibodies, in the treatment of B cell lymphomas and leukemias.



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It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001

On this record, it is reasonable to conclude that the same patient in need is being administered the same neutralizing anti-CD40 and anti-CD20 antibodies to treat various neoplastic disorders and diseases by the same mode of administration in the same or nearly the same effective amounts in both the instant claims and the prior art reference.

Again, applicant's arguments have not been found persuasive.

8. Claims 1-11, 13-18, 32-39 and 46-49 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Hanna et al. (US 2001/0018041 A1) in view of Siegall et al. (U.S. Patent No. 6,843,989) and Grillo-Lopez (U.S. Patent No. 6,455,043)

and in further view of Armitage et al. (U.S. Patent No. 5,674,492 cited in paragraphs [0013] and [0104] of Hanna et al.) and Benoit et al. (Immunopharmacology 35: 129-139, 1996) (1449; #59),

and in further evidence of the referenced teachings of agonistic anti-CD40 are acknowledged by page 2, paragraph 1 of the instant specification and paragraphs [0005] and [0036] of Fanslow et al., US 2005/0129689 A1) essentially for the reasons of record.

Applicant's arguments, filed 09/12/2007, in conjunction with certain legal citations, have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal concerning the teachings of Hanna et al. are essentially the same as that addressed above in the rejection under 3 USC 102 and reiterated herein for applicant's convenience.

Applicant argues that Hanna et al. requires the use of an anti-CD40L antibody antagonists, wherein applicant's claims as amended do not require a CD40L antagonist as defined by the prior art.

However, as pointed out previously, Hanna is not limited to the use of anti-CD40L antibody antagonists (as apparently defined and asserted by applicant) to treat malignancies.

Again, applicant is reminded that Hanna also contemplates the particular combination of anti-CD20 antibodies and anti-CD40 antibodies. See paragraph [0104] on page 10 of Hanna.

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Paragraphs [0013] and [0104] of Hanna et al. contemplates the anti-CD40 antibodies taught by Armitage et al. (U.S. Patent No. 5,674,492).

Armitage et al. teach anti-CD40 antibodies, including the M2 and M3 antibodies (See entire document).

For example, page 2, paragraph 1 of the instant specification discloses that:

"CD40 stimulation by mAb M2 and M3 inhibits growth of several B-cell lymphomas and induces regression of several B-cell lymphomas and induces regression of established tumors in vivo (Funakoshi et al., (1994) Blood 83: 2787-2794; Funakoshi et al. J. Immunol., (1996) 19: 93-101).

Fanslow et al. US 2005/0129689 A1) describes the antibodies referenced in U.S. Patent No. 5,674,492, namely the M2 and M3 antibodies as agonistic anti-CD40 antibodies as those antibodies that mimic the biological effects of CD40L are useful in the treatment of disease characterized by neoplastic cells that express CD40 such as B lymphomas, melanomas and carcinomas,

Again, certain anti-CD40 antibodies referenced by Hanna et al. are the same anti-CD40 antibodies taught by U.S. Patent No. 5,674,492, which is referenced in paragraphs [0013] and [0104] of Hanna et al.

Therefore, in contrast to applicant's assertions that Hanna et al. does not teach anti-CD40 antibodies that stimulate CD40, as currently recited in the instant claims,

Hanna et al. does teach the use of agonistic anti-CD40 antibodies that can stimulate CD40, as currently recited in the instant claims, including its combination with anti-CD20 antibodies, in the treatment of B cell lymphomas and leukemias.

Applicant does not appear to address or distinguish the teachings of Hanna's teaching of agonistic anti-CD40 antibodies M2 and M3 from the description of the instant specification of the same M2 and M3 antibodies that can inhibit the growth of several B-cell lymphomas and induces regression of several B-cell lymphomas and induces regression of established tumors in vivo application.

Products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Therefore, Hanna et al. does teach the use of anti-CD40 antibodies, including its combination with anti-CD20 antibodies, in the treatment of B cell lymphomas and leukemias.

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Applicant asserts that the instant claims are unexpected and surprising in the teachings of Benoit et al. because the instant do not require a crosslinking agent for therapeutic activity.

In contrast to applicant's limited reading of the teachings of Benoit et al. and while Benoit et al. may have employed crosslinking antibodies,

Benoit et al. was provided to address applicant's arguments concerning motivation of combining anti-CD40 antibodies with anti-CD20 antibodies in the treatment of B cell lymphomas.

Benoit et al. teach the increased inhibition of proliferation of B cell lymphomas following ligation of CD40, and CD20, for example (see entire document, including Abstract and Discussion).

The anti-CD40 antibody was the known G28-5 anti-CD40 antibody (see Antibodies and reagents on page 130, column 2).

Benoit et al. in combination with the other teachings of the prior art, one of ordinary skill in the art would have been motivated to target CD20 and CD40 in the treatment of neoplastic diseases and disorders at the time the invention was made.

Further, applicant does not appear to address the clear teachings of Siegall which teaches methods of treating cancer, including leukemias, lymphomas (e.g. non-Hodgins lymphoma), solid tumor and multiple myeloma (e.g. see Therapeutic Uses, including Table 1 on columns 22-23 and Claims) with CD40-specific antibodies, including the S2C6 CD40-specific antibody of the instant invention (see entire document, including Claims).

The anti-CD40 S2C6 antibody is the same SGN-14 antibody / antibody specificity of the instant methods.

For the purposes of searching for and applying prior art under **35 U.S.C. 102 and 103**, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG Industries v. Guardian Industries, 48 USPQ2d 1351, 1355 (Fed. Cir. 1998).

It is noted that the claimed methods recite "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts.

See MPEP 2111.03.

Further, it is noted the current claims recited further comprising cytotoxic and chemotherapeutic agents as well as cytotoxic antibody conjugates that differ in structure and modes of action from antibodies that stimulate CD40 in the claimed methods of treating neoplastic diseases and disorders.

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Therefore, the instant claims are met by any prior teaching of combining anti-CD40L antibodies with anti-CD20 and anti-CD40 antibodies, as broadly encompassed by the claimed methods.

Further, as noted previously, the prior art is directed towards effective treatment of the same malignancies with the same anti-CD40 antibodies and anti-CD20 antibodies encompassed by the instant claims.

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001)

On this record, it is reasonable to conclude that the same patient in need is being administered the same neutralizing anti-CD40 and anti-CD20 antibodies to treat various neoplastic disorders and diseases by the same mode of administration in the same or nearly the same effective amounts in both the instant claims and the prior art reference.

The following of record is reiterated for applicant's convenience.

Siegall teach methods of treating cancer, including leukemias, lymphomas (e.g. non-Hodgkins lymphoma), solid tumor and multiple myeloma (e.g. see Therapeutic Uses, including Table 1 on columns 22-23 and Claims) with CD40-specific antibodies, including the S2C6 CD40-specific antibody of the instant invention (see entire document, including Claims)

Grillo-Lopez also teach treating various tumors with CD20-specific antibodies (See entire document) and teachings the expression of CD20 on multiple myeloma (e.g. see columns 15-16, overlapping paragraph) in addition to leukemias and lymphomas (e.g. see Field of the Invention on column 1 and Detailed Description of the Invention and Claims).

Benoit et al. was provided to address applicant's arguments concerning motivation of combining anti-CD40 antibodies with anti-CD20 antibodies in the treatment of B cell lymphomas.

Benoit et al. teach the increased inhibition of proliferation of B cell lymphomas following ligation of CD40, and CD20, for example (see entire document, including Abstract and Discussion).

The anti-CD40 antibody was the known G28-5 anti-CD40 antibody (see Antibodies and reagents on page 130, column 2).

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Given both the therapeutic use of CD40-specific antibodies and CD20-specific antibodies to treat various neoplastic diseases, including leukemias, lymphomas, myelomas and solid tumors, the ordinary artisan would have been motivated to combine the two antibody specificities as taught by Hanna et al. in combination therapies to target other neoplastic tissues in order to increase the efficacy of cancer treatment. As taught by all of the prior art references, combination therapies, including combination with antibodies or combination of antibodies with more traditional chemotherapy and radiotherapy were well known and practiced by the ordinary artisan at the time the invention was made to increase efficacy of treatment and to minimize toxic effects of such treatment in order to meet the needs of the patients (see Detailed Descriptions of Hanna et al., Siegall and Grillo-Lopez). From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Also, as pointed out previously in response to applicant's arguments of record and reiterated that there is no motivation or suggestion to combine the references,

the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir. 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case the teachings of the prior art do provide for the use of anti-CD40 antibodies in the treatment of certain neoplastic disorders and diseases and do indicate success in treating neoplastic disorders and diseases with anti-CD40 antibodies in combination with anti-CD20 antibodies that would have led one of ordinary skill in the art at the time the invention was made to combine the references to solve a well known problem in the art. The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983). See MPEP 2144.

Again, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the combination of the prior art disclosure in motivating the ordinary artisan to administer anti-CD20 antibodies and anti-CD40 antibodies to treat patients with neoplastic diseases or conditions.

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"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Given that the prior art goal was to treat patients with neoplastic diseases or conditions with anti-CD20 antibodies and anti-CD40 antibodies,

incorporating the combination of anti-CD20 antibodies and anti-CD40 antibodies in therapeutic regimens with patients with neoplastic diseases or disorders would have been routine to the ordinary artisan at the time the invention was made and therefore obvious in designing such therapeutic methods to treat said neoplastic diseases and disorders.

Applicant's arguments have not been found persuasive

9. No claims are allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

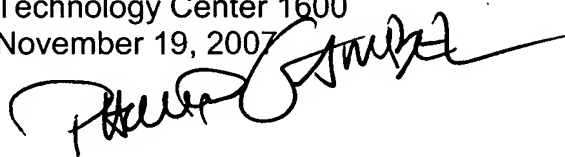
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, Ph.D., J.D.

Primary Examiner

Technology Center 1600

November 19, 2007

A handwritten signature in black ink, appearing to read "Phillip Gambel", is written over the typed name and date.